

## **I. Claim Listing**

---

Claims 1-16 (Withdrawn)

131  
Claim 17 (Original): A method for identifying an inhibitor of a microbial isocitrate lyase enzyme (ICL), comprising:

- (a) defining the catalytic active site of ICL from the atomic coordinates selected from the group consisting of the atomic coordinates for the apo-ICL of FIG. 5 (Protein Data Bank accession code 1F61), the atomic coordinates for the ICL-3-brompyruvate complex of FIG. 6 (Protein Data Bank accession code 1F8M) and the atomic coordinates for the ICL-3-nitropropionate complex of FIG. 7 (Protein Data Bank accession code 1F8I); and
- (b) identifying a non-native substrate compound that fits said active site and thereby inhibits said microbial isocitrate lyase enzyme.

Claim 18 (Original): A method for identifying an inhibitor of a microbial ICL, comprising:

- (a) obtaining atomic coordinates of ICL, wherein said atomic coordinates are selected from the group consisting of the apo-ICL atomic coordinates of FIG. 5 (Protein Data Bank accession code 1F61), the ICL-3-brompyruvate complex atomic coordinates of FIG. 6 (Protein Data Bank accession code 1F8M) and the ICL-3-nitropropionate complex atomic coordinates of FIG. 7 (Protein Data Bank accession code 1F8I);
- (b) defining the catalytic active site of ICL from said atomic coordinates; and
- (c) identifying a non-native substrate compound that fits said catalytic active site, wherein a non-native substrate compound that fits said active site is indicative of an inhibitor of a microbial ICL.

Claim 19 (Original): The method of claim 18, wherein said non-native substrate compound that fits said catalytic active site is identified by selecting a candidate compound and confirming that said candidate compound inhibits said microbial ICL.

Claim 20 (Original): A method for identifying an inhibitor of a microbial ICL, comprising:

- (a) obtaining atomic coordinates of ICL, wherein said atomic coordinates are selected from the group consisting of the apo-ICL atomic coordinates of FIG. 5 (Protein Data Bank accession code 1F61), the ICL-3-bromopyruvate complex atomic coordinates of FIG. 6 (Protein Data Bank accession code 1F8M) and the ICL-3-nitropropionate complex atomic coordinates of FIG. 7 (Protein Data Bank accession code 1F8I);
- (b) defining the catalytic active site of ICL from said atomic coordinates;
- (c) selecting a candidate compound by identifying a non-native substrate compound that fits said catalytic active site; and
- (d) contacting said microbial ICL with said candidate compound under conditions effective for ICL activity, wherein a candidate compound that inhibits the activity of said microbial ICL is confirmed as an inhibitor of said microbial ICL.

Claim 21 (Original): The method of claim 20, wherein said candidate compound is selected from consideration of a database of compounds.

Claim 22 (Original): The method of claim 20, wherein said candidate compound is selected by *de novo* design.

Claim 23 (Original): The method of claim 20, wherein said candidate compound is selected by design starting from a known inhibitor.

Claim 24 (Original): The method of claim 20, wherein said candidate compound is selected by identifying a compound intended to interact with at least one of ICL amino acids His 193, Asn 313, Ser 315 or Ser 317 according to FIG. 5, FIG. 6 or FIG. 7.

31  
Claim 25 (Original): The method of claim 24, wherein a candidate compound intended to interact with at least one of said ICL amino acids His 193, Asn 313, Ser 315 or Ser 317 is selected by employing computational means to perform a fitting operation between said

candidate compound and a binding pocket defined by said amino acids within a root mean square deviation from the backbone atoms of said amino acids of not more than 1.5 angstroms.

Claim 26 (Original): The method of claim 20, wherein the inhibitor so identified inhibits a mycobacterial ICL.

Claim 27 (Original): The method of claim 26, wherein the inhibitor so identified inhibits *M. tuberculosis* ICL.

Claim 28 (Original): The method of claim 20, wherein the inhibitor so identified inhibits a fungal ICL.

Claim 29 (Original): The method of claim 20, wherein the inhibitor so identified inhibits said microbial ICL by changing the structure of said active site from the open conformation to the closed conformation.

Claim 30 (Original): The method of claim 20, wherein the inhibitor so identified is a competitive inhibitor.

Claim 31 (Original): The method of claim 20, wherein the inhibitor so identified is a non-competitive or uncompetitive inhibitor.

Claim 32 (Original): The method of claim 20, further comprising purifying or synthesizing the inhibitor so identified.

Claim 33 (Original): The method of claim 20, further comprising formulating the inhibitor so identified in a pharmaceutically acceptable formulation.

Claim 34 (Original): The method of claim 33, wherein said pharmaceutically acceptable formulation further comprises at least a second antimicrobial agent.

Claims 35-45 (Withdrawn)